set of residues on C-TRAF2 required for N-TRADD binding. This N-TRADD binding site on C-TRAF2 would overlap with the CD40 binding site.

In the Claims:

Please rewrite Claim 2 as follows:

2. (amended) The solution of Claim 1, wherein the N-terminal domain of TNFR-1 associated death domain protein comprises amino acid residues 1-169 in SEQ ID NO:1.

Please attach at the end of the application pages 1-3 of the Sequence Listing (attached hereto as Exhibit E).

REMARKS

By this Amendment, Applicants have amended the specification and Claim 2 to refer to sequence identifiers, as required by the Sequence Rules, and to add the Sequence Listing. The amendments to the specification and Claim 2 are supported by the application as originally filed. Accordingly, entry of the amendments to the specification and Claim 2 is respectfully requested.

Compliance with Sequence Rules

The July 13, 2001 Notice to File Missing Parts of Nonprovisional Application (Exhibit A) indicated that the application did not comply with the Sequence Rules. In response thereto, Applicants attach herewith Exhibit E, consisting of pages 1-3 of the Sequence Listing. Also enclosed is a computer-readable form containing the Sequence

Listing (Exhibit F). Additionally, the specification and Claim 2 have been amended to refer to the sequence identifiers, as required by the Sequence Rules.

The undersigned attorney hereby certifies that the information recorded in computer-readable form is identical to the written Sequence Listing, is supported by the application as filed, and does not introduce new matter into the application as filed. In view of the above-noted amendments and these remarks, applicants respectfully submit that they have complied with the Sequence Rules. Accordingly, entry of the Sequence Listing is respectfully requested.

No fee is deemed necessary in connection with the filing of this Amendment. If any fee is required to preserve the pendency of the application, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 01-1785.

Respectfully submitted,

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Attorneys for Applicants
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New York, New York 10016
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Dated: September 13, 2001
New York, New York

By: _____
Craig J. Arnold
Registration No. 34,287

SCHEDULE A

REDLINED VERSION

In the Specification:

Please replace the paragraph at page 7, line 23 as follows:

Figure 1 depicts the 169 amino acid sequence **(SEQ ID NO:1)** encoding the N-terminal domain of human TNFR-1 associated death domain protein (wherein said N-terminal domain is referred to herein as "N-TRADD"), with the secondary structures noted below.

Please replace the paragraph at page 30, line 8 as follows:

The CD40 peptide (SNTAAPVQETLHG-OH) **(SEQ ID NO:2)** was synthesized by using fluorenylmethoxycarbonyl (Fmoc) solid-phase methods and purified by reverse-phase HPLC.

Please replace the paragraph at page 34, line 14 as follows:

Inhibition of N-TRADD/C-TRAF2 by CD40-derived peptide: Recent reports on a C-TRAF2 binding peptide derived from CD40 receptor (Pullen, *et al.*, Biochemistry 37: 11836-11845, 1998; Sato, *et al.*, FEBS Lett 358: 113-118, 1995; Nakano, *et al.*, J. Biol. Chem. 271: 14661-14664, 1996) led the inventors to study the effect of this peptide on the N-TRADD/C-TRAF2 interaction. CD40 belongs to the TNF receptor family and has been shown to interact with several TRAF family members by yeast two hybrid analysis and co-precipitation assays (Pullen, *et al.*, J. Biol. Chem. 274: 14246-14254, 1999; Pullen, *et al.*, Biochemistry 37: 11836-11845, 1998; Cheng, *et al.*, Science 267: 1494-1498, 1995).

In particular, full length TRAF2 has been shown to interact directly with the CD40 cytoplasmic domain (Pullen, *et al.*, Biochemistry 37: 11836-11845, 1998). The binding site of CD40 for TRAF2 was defined by peptide mapping where the shortest CD40 sequence that TRAF2 recognized was a five amino acid peptide with the sequence PVQET (amino acid residues 6-10 of SEQ ID NO:2). The crystal structure of C-TRAF2 (311-501) with a peptide derived from CD40 with sequence YPIQET (SEQ ID NO:3) (designated CD40-p1) (McWhirter, *et al.*, Proc. Natl. Acad. Sci. USA 96: 8408-8413, 1999) (Published with Protein Data Bank at Accession No. 1QSC, and expressly incorporated herein by reference) shows that it binds each of the TRAF2 monomers in the C-TRAF2 trimer complex. Comparison with the structure of the peptide from TNFR-2 in complex with C-TRAF2 (Park, *et al.*, Nature 398: 533-538, 1999), which has a different consensus sequence (QVPFSKEEC) (SEQ ID NO:4), reveals similar affinities and conformations (McWhirter, *et al.*, Proc. Natl. Acad. Sci. USA 96: 8408-8413, 1999). However, despite similar backbone contacts, the two peptides are slightly shifted in the binding site, where CD40 peptide makes many more complementary contacts with C-TRAF2 than does the TNFR-2-derived peptide.

Please replace the paragraph at page 35, line 12 as follows:

In the instant studies, the interaction between a 13-mer peptide derived from CD40 (a longer version of CD40-p1, with sequence SNTAAPVQETLHG (SEQ ID NO:2)) with C-TRAF2 was characterized, as well as its effect on the N-TRADD/C-TRAF2 interaction. BIAcore studies show that the peptide binds to C-TRAF2 with an affinity of ~1.0 mM (data not shown). In addition the peptide was also able to compete for the binding of N-TRADD to C-TRAF2, with an IC50 of ~ 1mM.

Please replace the paragraph at page 36, line 27 as follows:

Based on previous studies (Arch, *et al.*, Genes Dev 12: 2821-2830, 1998; Park, *et al.*, Nature 398: 533-538, 1999; McWhirter, *et al.*, Proc. Natl. Acad. Sci. USA 96: 8408-8413, 1999), C-TRAF2 can recognize at least two different sequence motifs, SXXE (SEQ ID NO:5) in the case of TNFR2 and PXQXT (SEQ ID NO:6) for CD40. Although the two peptides make similar backbone contacts, each peptide makes different additional unique contacts with C-TRAF2, suggesting the presence of distinct recognition sites. Neither consensus sequence is present in N-TRADD, implying that there may be another set of residues on C-TRAF2 required for N-TRADD binding. This N-TRADD binding site on C-TRAF2 would overlap with the CD40 binding site.

In the Claims:

Please rewrite Claim 2 as follows:

2. (amended) The solution of Claim 1, wherein the N-terminal domain of TNFR-1 associated death domain protein comprises amino acid residues 1-169 ~~of Figure 1~~ in SEQ ID NO:1.